

Appl. No. : 104,340  
Filed : June 25, 1998

The Claims have been amended to more precisely recite the claimed invention. Claims 38-39 and 42-43 have been canceled, Claim 44 was added, and Claims 1-12, 20, 35-37, and 40-41 were amended. Support for the amended and added claims can be found in the Claims and Specification as filed. Specifically, support for amended Claim 1 can be found on page 6 of the Specification, lines 10-16. As a result of the amendment, Claims 1-12, 20, 35-37, 40-41, and 44 are presented for examination.

**Rejection under 35 U.S.C. §112, second paragraph**

The Examiner has rejected Claims 1-8, 11-12, 20, 34, and 37 under 35 U.S.C. §112, second paragraph, as indefinite. More specifically the Examiner believes:

Claims 1, 2, 4, 5, 11, and 12 are indefinite because it is not clear what comprises "an Eph family RTK". However, this term has been removed from amended claim 1 and replaced with "an EPH receptor tyrosine kinase gene" as suggested by the Examiner.

Claims 1-4, 20, 34, and 37 are believed indefinite because it is not clear what constitutes the "ligand-binding domain" of an Eph family RTK. However, the term "ligand binding domain" has been removed from the claims.

Claims 4-7, 11 and 37 are believed indefinite because it is not clear what amino acid sequence the "ligand-binding domain" is referring to. Further, in Claim 11, the Examiner believes that since the term is unclear, it is unclear what subsequence one is referring to.

Applicants have amended Claim 1 to recite "an amino acid sequence encoded by exon I, II or III". Applicants believe this term to be definite because one of skill in the art could easily determine what comprises exon I, II or III. Further, in the dependent claims the specific SEQ ID NOS referring to the specific EPH receptor tyrosine kinase gene are presented (see Claims 35, 36, and 37).

Claim 11 is also believed indefinite because the Examiner believes the term "homolog" is indefinite. However, the term has been removed from the claim.

In view of the amendments, Applicants believe the claims to be definite and respectfully request withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

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**Rejection under 35 U.S.C. §112, first paragraph**

The Examiner has rejected Claims 1-8, 11-12, 20, 34, and 37 under 35 U.S.C. §112, first paragraph, because the Examiner believes that the Specification, while being enabling for an isolated polypeptide of SEQ ID NO:4 or 5, does not reasonably provide enablement for other polypeptides.

However, referring to the Rule 132 Declaration, the fundamental discovery of the Exon III-encoded ligand binding domain and the contribution of exon II-encoded sequence, first described in the instant specification, is now accepted as being relevant to all Eph family receptor tyrosine kinases, from invertebrates to humans. In studies published subsequent to the filing date of the instant application all of the predictions as to the generalizable correlation between exon structure and ligand binding as first set for the in the instant Specification have held true.

In other words, the Specification teaches a principle that can readily be put into practical effect without undue experimentation on the part of the skilled person. The relevant exon-encoded domain can be identified by exon/intron mapping techniques as set forth in Example 1, or by sequence alignment as is well understood in the art. A clear teaching of the present invention is that exons I, II, and III of Eph family RTK genes are structurally-defined elements which correlate with structural domains of the encoded polypeptide. The exon III- encoded domain is essential to LERK binding. Furthermore, at page 7 lines 6-8 it is stated that sequences flanking the exon III-encoded domain may form part of the ligand-binding domain. These are, by definition, exon II-encoded amino acids (exon IV sequences were never considered to be important), a prediction which is fully supported by subsequent structural studies in D23 for example.

Therefore, without exception, the teaching of the instant specification enables the skilled person to readily isolate an exon III, II and III, or I, II, and III-encoded nucleotide sequence which encodes a polypeptide capable of binding a LERK, as recited by Claim 1 or Claim 2, for example.

In addition, the Examiner is mistaken in stating that the specification only teaches binding of LERK7. In Example 4 at pages 38 and 39, it is explicitly stated that the polypeptide encoded by exons I-III of the HEK gene hierarchically binds LERK7, LERK8, LERK4 and LERK5 (in order of decreasing affinity) to the exclusion of LERKS 1 and 2. Therefore, the Specification is not only enabling with respect to LERK7.

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**Rejection under 35 U.S.C. §102**

The Examiner has rejected Claims 1-12, 20, 34-41 under 35 U.S.C. §102(a) as being anticipated by Boyd et al (Ref B, U.S. Patent No. 5,674,691). The Examiner believes that Boyd teaches the polynucleotide of SEQ ID NOS:1-4 encoded the polypeptide of SEQ ID NOS: 5-8. The sequences disclosed by Boyd et al are for HEK. The receptor-type tyrosine kinase is identified as a member of the eph/elk family.

However, the amended claims now render moot the novelty objection based on U.S. patent 5,674,691.

Claim 1 recites a polypeptide consisting essentially of an amino acid sequence which is encoded by exon III of an Eph family receptor tyrosine kinase gene, or which is encoded by exon III and exon II, or by exon III, II and I. This claim necessarily excludes the extracellular domain of HEK. In addition, the cited patent does not teach or suggest the gene arrangement of the exons or which exons are involved in ligand binding. The cited patent only sets forth the full-length sequence of the HEK tyrosine kinase.

Claim 2 now recites a polypeptide comprising the amino acid sequences as per Claim 1, while specifically excluding the extracellular domain of HEK, as described in U.S. patent 5,674,691.

Claims 5 and 6 are restricted to SEQ ID NO:4 and exclude the extracellular domain of HEK in a similar fashion to Claims 1 and 2.

Claim 14 is directed to a nucleic acid which hybridizes with SEQ ID NO:5 under high stringency wash conditions. The conditions are calculated to allow hybridization of sequences sharing no less than 80% identity with SEQ ID NO:5. The functional limitation is that the hybridizing sequence encodes a polypeptide excluding the extracellular domain of Eph family RTK.

In summary, U.S. patent 5,674,691 merely suggested that the extracellular domain of HEK may bind ligand. The ligand was not disclosed. There was no disclosure of the exon III-encoded domain required for ligand binding, and the methods employed by the present inventors were not contemplated in U.S. patent 5,674,691.

In view of the above amendments, argument and the enclosed Declaration, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §102(a).

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**Conclusion**

In light of the Applicant's amendments to the claims and the specification as well as the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

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